



4160-01-P

DEPARTMENT OF HEALTH AND HUMAN SERVICES

Food and Drug Administration

[Docket No. FDA-2011-D-0605]

Draft Guidance for Industry on Scientific Considerations in Demonstrating Biosimilarity to a Reference Product; Availability

AGENCY: Food and Drug Administration, HHS.

ACTION: Notice.

SUMMARY: The Food and Drug Administration (FDA) is announcing the availability of a draft guidance for industry entitled "Scientific Considerations in Demonstrating Biosimilarity to a Reference Product." This draft guidance is intended to assist sponsors in demonstrating that a proposed therapeutic protein product is biosimilar to a reference product for the purpose of submitting a marketing application through an abbreviated licensure pathway. This draft guidance gives an overview of FDA's approach to determining biosimilarity.

DATES: Although you can comment on any guidance at any time (see 21 CFR 10.115(g)(5)), to ensure that the Agency considers your comment on this draft guidance before it begins work on the final version of the guidance, submit either electronic or written comments on the draft guidance by [INSERT DATE 60 DAYS AFTER DATE OF PUBLICATION IN THE FEDERAL REGISTER].

ADDRESSES: Submit written requests for single copies of the draft guidance to the Division of Drug Information, Center for Drug Evaluation and Research, Food and Drug Administration, 10903 New Hampshire Ave., Bldg. 51, rm. 2201, Silver Spring, MD 20993-0002; or the Office of Communication, Outreach and Development (HFM-40), Center for Biologics Evaluation and

Research, Food and Drug Administration, 1401 Rockville Pike, suite 200N, Rockville, MD 20852-1448. Send one self-addressed adhesive label to assist that office in processing your requests. See the SUPPLEMENTARY INFORMATION section for electronic access to the draft guidance document.

Submit electronic comments on the draft guidance to <http://www.regulations.gov>.

Submit written comments to the Division of Dockets Management (HFA-305), Food and Drug Administration, 5630 Fishers Lane, rm. 1061, Rockville, MD 20852.

FOR FURTHER INFORMATION CONTACT:

Sandra Benton,
Center for Drug Evaluation and Research,
Food and Drug Administration,
10903 New Hampshire Ave.,
Bldg. 51, rm. 6340,
Silver Spring, MD 20993-0002,
301-796-1042;

or

Stephen Ripley,
Center for Biologics Evaluation and Research (HFM-17),
Food and Drug Administration,
1401 Rockville Pike, suite 200N,
Rockville, MD 20852-1448,
301-827-6210.

SUPPLEMENTARY INFORMATION:

I. Background

FDA is announcing the availability of a draft guidance for industry entitled "Scientific Considerations in Demonstrating Biosimilarity to a Reference Product." This draft guidance is intended to assist sponsors in demonstrating that a proposed therapeutic protein product is "biosimilar"¹ to a reference product for the purpose of submitting a marketing application through the abbreviated licensure pathway under section 351(k) of the Public Health Service Act (PHS Act) (42 U.S.C. 262(k)).

The Biologics Price Competition and Innovation Act of 2009, enacted as part of the Affordable Care Act (Public Law 111-148) on March 23, 2010, created an abbreviated licensure pathway under section 351(k) of the PHS Act for biological products demonstrated to be biosimilar to, or interchangeable with, a reference product. Under this abbreviated licensure pathway, FDA will license a proposed biological product submitted under section 351(k) of the PHS Act if FDA "determines that the information submitted in the application * * * is sufficient to show that the biological product is biosimilar to the reference product * * * " and the 351(k) applicant (or other appropriate person) consents to an inspection of the facility that is the subject of the application (i.e., a facility in which the proposed biological product is manufactured, processed, packed, or held).² The draft guidance gives an overview of FDA's approach to determining biosimilarity. FDA intends to consider the totality of the evidence submitted in a 351(k) application and is recommending that sponsors use a stepwise approach in their

¹ In section 7002(b)(3) of the Patient Protection and Affordable Care Act (Affordable Care Act), Public Law 111-148, "biosimilar" or "biosimilarity" means "that the biological product is highly similar to the reference product notwithstanding minor differences in clinically inactive components," and that "there are no clinically meaningful differences between the biological product and the reference product in terms of the safety, purity, and potency of the product."

development of biosimilar products. The draft guidance discusses important scientific considerations in demonstrating biosimilarity, including:

- A stepwise approach to demonstrating biosimilarity, which can include a comparison of the proposed therapeutic protein product and the reference product with respect to structure, function, animal toxicity, human pharmacokinetics and pharmacodynamics, clinical immunogenicity, and clinical safety and effectiveness;
- The totality-of-the-evidence approach that FDA will use to review applications for biosimilar products; and
- General scientific principles in conducting comparative structural and functional analysis, animal testing, human pharmacokinetics and pharmacodynamics studies, clinical immunogenicity assessment, and clinical safety and effectiveness studies (including clinical study design issues).

This draft guidance is being issued consistent with FDA's good guidance practices regulation (21 CFR 10.115). The draft guidance, when finalized, will represent the Agency's current thinking on scientific considerations in demonstrating biosimilarity to a reference product. It does not create or confer any rights for or on any person and does not operate to bind FDA or the public. An alternative approach may be used if such approach satisfies the requirements of the applicable statutes and regulations.

II. Comments

Interested persons may submit to the Division of Dockets Management (see ADDRESSES) either electronic or written comments regarding this document. It is only

² Section 7002(a)(2) of the Affordable Care Act, adding section 351(k)(3) of the PHS Act (citing section 351(a)(2)(C) of the PHS Act).

necessary to send one set of comments. Identify comments with the docket number found in brackets in the heading of this document. Received comments may be seen in the Division of Dockets Management between 9 a.m. and 4 p.m., Monday through Friday.

III. The Paperwork Reduction Act

This draft guidance describes information collection provisions that are subject to review by the Office of Management and Budget (OMB) under the Paperwork Reduction Act of 1995 (the PRA) (44 U.S.C. 3501-3520). In particular, the draft guidance refers to information collections related to the submission of 351(k) application. In accordance with the PRA, FDA is soliciting public comment, in a separate document published elsewhere in this issue of the Federal Register (see “Agency Information Collection Activities: Proposed Collection; Comment Request; General Licensing Provisions; Section 351(k) Biosimilar Applications”) on the information collection associated with the submission of a 351(k) application. FDA will also seek OMB approval for this information collection.

In addition, this draft guidance references other information collections that are already approved by OMB and are not expected to change as a result of the draft guidance. This includes information collections related to the the submission of (1) an investigational new drug application, which is covered under 21 CFR part 312 and approved under OMB control number 0910-0014; (2) a new drug application, which is covered under 21 CFR 314.50 and approved under OMB control number 0910-0001; (3) a biologics license application, which is covered under 21 CFR part 601 and approved under OMB control number 0910-0338; and (4) labeling, which is covered under 21 CFR 201.57 and approved under OMB control number 0910-0572.

IV. Electronic Access

Persons with access to the Internet may obtain the document at either

<http://www.fda.gov/Drugs/GuidanceComplianceRegulatoryInformation/Guidances/default.htm>,

<http://www.fda.gov/BiologicsBloodVaccines/GuidanceComplianceRegulatoryInformation/default.htm>, or <http://www.regulations.gov>.

Dated: February 9, 2012.

Leslie Kux,

Acting Assistant Commissioner for Policy.

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